Heart failure (HF) is a major epidemic and significant public health burden in our aging society. In recent years, much attention has turned to the role of mineral and bone metabolism in HF, specifically vitamin D deficiency and hyperparathyroidism, which is common in elderly populations. Parathyroid hormone (PTH), a peptide hormone of 84 amino acids, is secreted by the parathyroid glands to promote Vitamin D activation and acts to control calcium homeostasis. The release of PTH is mediated by serum calcium, phosphorus, and vitamin D metabolites. Chronic PTH elevation with low serum calcium (secondary hyperparathyroidism) is usually secondary to renal impairment or vitamin D deficiency. As such, the role of PTH as a key regulatory hormone in bone health and mineral homeostasis is well established. However, excess PTH may have possible effects beyond the regulation of calcium homeostasis. In recent years, there has been mounting evidence regarding the contribution of PTH to the pathogenesis of HF. PTH receptors are expressed in the vessel walls and the myocardium, and in vitro studies have shown that PTH induces hypertrophy of cardiomyocytes. Experimental and clinical studies have suggested that elevated PTH enhances myocardial fibrosis, calcification, and hypertrophy, which may eventually lead to HF. In epidemiological studies, PTH is increased in patients with HF and has shown to be independently associated with hospitalization for HF in these patients. Population studies have shown PTH elevation to be associated with major risk factors for HF, including hypertension, left ventricular hypertrophy (LVH), atrial fibrillation (AF), myocardial dysfunction (N-terminal probrain natriuretic peptide [NT-proBNP]), and LV mass. Although several studies have shown PTH to

Original Article

Elevated Parathyroid Hormone, But Not Vitamin D Deficiency, Is Associated With Increased Risk of Heart Failure in Older Men With and Without Cardiovascular Disease

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Background—Hyperparathyroidism and low vitamin D status have been implicated in the pathogenesis of heart failure (HF). We examined the prospective associations between parathyroid hormone (PTH), circulating 25-hydroxyvitamin D, and markers of mineral metabolism and risk of incident HF in older men with and without established cardiovascular disease.

Methods and Results—Prospective study of 3731 men aged 60 to 79 years with no prevalent HF followed up for a mean period of 13 years, in whom there were 287 incident HF cases. Elevated PTH (≥55.6 pg/mL; top quarter) was associated with significantly higher risk of incident HF after adjustment for lifestyle characteristics, diabetes mellitus, blood lipids, blood pressure, lung function, heart rate, renal dysfunction, atrial fibrillation, forced expiratory volume in 1 second, and C-reactive protein (hazards ratio, 1.66; 95% confidence interval, 1.30–2.13). The increased risk was seen in both men with and without previous myocardial infarction or stroke (hazards ratio, 1.72; 95% confidence interval, 1.07–2.76; hazards ratio, 1.70; 95% confidence interval, 1.25–2.30, respectively). Elevated PTH was significantly associated with N-terminal probrain natriuretic peptide, a marker of left ventricular wall stress. By contrast, 25-hydroxyvitamin D and other markers of mineral metabolism including serum calcium and phosphate showed no significant association with incident HF after adjustment for age.

Conclusions—Elevated PTH, but not 25-hydroxyvitamin D or other markers of mineral metabolism, is associated with increased risk of HF in both older men with and without myocardial infarction/stroke. This increased risk was not explained by its association with known risk factors for HF. Further studies are now needed to elucidate the mechanisms underlying this association.

Key Words: heart failure ■ parathyroid hormone ■ vitamin D

Received March 6, 2014; accepted July 28, 2014.

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Circ Heart Fail is available at http://circheartfailure.ahajournals.org

DOI: 10.1161/CIRCHEARTFAILURE.114.001272
be associated with cardiovascular disease (CVD), many have not; few prospective studies have specifically examined the association between PTH and incident HF in the general population. Two prospective studies in older adults have shown PTH levels to be related to incident HF independent of known risk factors for HF, whereas 1 study conducted in middle-aged population showed the association to be present in obese subjects only. Moreover, whether PTH is associated with incident HF in older adults with established CVD, who are at high risk of HF, has not been studied. In contrast, the prospective association between vitamin D and HF has been studied in several population studies, but the results have been equivocal, with some prospective studies showing an association between low vitamin D status and HF; others have shown null results.

We, therefore, examined the relationships between PTH and 25-hydroxyvitamin D (25OHD, a marker of circulating active vitamin D levels), as well as markers of mineral metabolism (calcium and phosphate) and incident HF in older men with and without established CVD (myocardial infarction [MI] or stroke).

### Methods

The British Regional Heart Study is a prospective study involving 7735 men aged 40 to 59 years drawn from 1 general practice in each of 24 British towns, who were screened between 1978 and 1980. The population studied was socioeconomically representative of British men and comprises predominantly white Europeans (>99%). In 1998 to 2000, all surviving men, then aged 60 to 79 years, were invited for a 20th-year follow-up examination. Ethical approval was obtained from all relevant local research ethics committees. All men completed a mailed questionnaire providing information on their lifestyle and medical history, had a physical examination, and provided a fasting blood sample. The samples were frozen and stored at −20°C on the day of collection and transferred in batches for storage at −70°C until thawed for vitamin D assay; they were then refrozen and thawed for PTH analysis. Thus, all samples were treated identically. Twelve-lead electrocardiograms were recorded using a Siemens Sicard 460 instrument and were analyzed using Minnesota Coding definitions at the University of Glasgow ECG core laboratory. The men were asked whether a doctor had ever told them that they had MI, HF, or stroke; details of their medications including use of statins and other cholesterol-lowering drugs were recorded at the examination. They were additionally asked whether they regularly took any vitamins or mineral tablets. In all, 4252 men had a measurement of PTH or 25OHD. Of these men, we excluded 112 others who had shown null results.

Cardiovascular Risk Factor Measurements at 1998 to 2000

Anthropometric measurements including body weight, height, and waist circumference were taken. Details of measurement and classification methods for smoking status, physical activity, social class, alcohol intake, blood pressure, blood lipids, and measures of lung function (forced expiratory volume in 1 second [FEV1]) in this cohort have been described. C-reactive protein was assayed by ultrasonic nephelometry (Dade Behring, Milton Keynes, United Kingdom). Estimated glomerular filtration rate (eGFR) (measure of renal function) was from serum creatinine using the equation eGFR=186×(creatinine)−1.154×(age)−0.203. Chronic kidney disease was defined as eGFR <60. NT-proBNP was determined using the Elecsys 2010 electrochemiluminescence method (Roche Diagnostics, Burgess Hill, United Kingdom). Electrocardiographic LVH was defined according to relevant Minnesota codes (codes 3.1 or 3.3). AF was defined according to Minnesota codes 8.3.1 and 8.3.3.

Plasma Vitamin D and Parathyroid Hormone

Measurement of 25OHD was performed on EDTA-anticoagulated plasma via a high-throughput method for the measurement of 25OHD and 25OH, using a gold-standard liquid chromatography-tandem mass spectrometry method following an automated solid-phase extraction procedure. Our method is calibrated and controlled using reagents from Chromsystems GmbH (Manchester, United Kingdom) and is currently in routine clinical use. The lower limit of sensitivity was 4 ng/mL for both 25OHD and total 25OHD. Results are reported as total 25OHD (25OHD plus 25OHD); virtually all participants had an undetectable 25OHD, which is commensurate with results observed in routine National Health Service use. Plasma PTH was measured by electrochemiluminescence using a clinically validated assay for intact PTH on the Elecsys 2010 (Roche Diagnostics) using the manufacturer’s calibrators and controls. Coefficients of variation were between 6.2% and 7.9% for 3 levels of control. Data on 25OHD were available in 3646 men, and data on PTH were available in 3728 men.

Follow-Up

All men have been followed up from initial examination (1978–1980) for cardiovascular morbidity, and follow-up has been achieved for 99% of the cohort. In the present analyses, all-cause mortality and morbidity events are based on follow-up from re-examination in 1998 to 2000 at mean age 60 to 79 years to June 2012. Survival times ended at the first HF event or when they were censored for death because of any cause, or the end of the follow-up period (June 2012), whichever occurred first. Information on death was collected through the established tagging procedures provided by the National Health Service registers. Fatal coronary heart disease (CHD) events were defined as death with CHD (International Classification of Diseases, Ninth Revision, codes 410–414) as the underlying code. A nonfatal MI was diagnosed according to World Health Organization criteria. Evidence of nonfatal MI and HF was obtained by ad hoc reports from general practitioners supplemented by biennial reviews of the patients’ practice records (including hospital and clinic correspondence) through to the end of the study period. Incident CHD included fatal CHD and nonfatal MI. Incident nonfatal HF was based on a doctor-confirmed diagnosis of HF from primary care medical records (including hospital and clinical correspondence). All cases were verified by a review of available clinical information from primary and secondary care records (symptoms, signs, investigations, and treatment response) to ensure they are consistent with current recommendations on HF diagnosis.

Incident fatal HF cases were those in which the diagnosis of HF was mentioned as the underlying cause of death at death certificates (International Classification of Diseases, Ninth Revision, code 428). Incident HF included both incident nonfatal HF (280 cases) and incident fatal HF (7 cases). We could obtain information on echocardiogram in only 49% (142 cases) of the 287 incident HF cases. Of these, 107 had HF with reduced ejection fraction (EF) and 35 had HF with preserved EF (HFpEF).

### Statistical Methods

The men were divided into equal quartiles based on the PTH and vitamin D distribution. Comparisons of baseline characteristics between the PTH groups were performed using the χ2 test for categorical variables and ANOVA for continuous variables. Spearman partial correlation coefficients were used to estimate the age-adjusted correlations between PTH and the biological markers, all fitted as continuous variables. All other analyses were based on PTH categories as mentioned. Kaplan–Meier curves and the log-rank test were used to evaluate differences in HF rates for the 4 PTH groups. Cox proportional hazards model was used to initially assess the age-adjusted hazards ratio (relative risk) in a comparison of quarters of PTH and 25OHD. Because of a threshold effect of PTH on incident HF, subsequent analyses were performed adjusting for potential confounders and mediators in a stepwise manner comparing the top quartile versus the rest. In multivariate analyses, smoking (never, long-term exsmokers [>15 years], recent exsmokers [<15 years], and current smokers), social class (manual versus nonmanual), physical activity (4 groups, diabetes mellitus [yes/no], use of antihypertensive treatment [yes/no], statins [yes/no], LVH [yes/no], and AF [yes/no]) were fitted as categorical variables. Systolic blood pressure, FEV1, eGFR, heart rate, C-reactive protein, and NT-proBNP were fitted as continuous variables. To assess whether
the association between PTH and incident HF may be because of the development of incident MI, which in turn results in increased risk of HF, we adjusted for incident CHD by fitting CHD as a time-dependent covariate. Subsidiary analysis was performed stratified by men with and without previous MI/stroke. We conducted a sensitivity analysis restricting cases to those with echocardiogram information on LVEF. All analyses were performed with SAS version 9.3 (SAS, Cary, NC).

Results

During the mean follow-up period of 13 years, there were 287 incident HF cases (rate, 7.3/1000 person-years) in the 3731 men with no diagnosed HF. Men with prevalent MI/stroke (n=528; 85 cases) had significantly higher rates of HF than men without MI (n=3203; 202 cases; 18.6 versus 5.8/1000 person-years; P<0.0001). The median level (interquartile range) of plasma vitamin PTH and 25OHD in the study population was 44.7 (36.1–56.0) and 19 (13–25) ng/mL, respectively. Severe 25OHD deficiency (<10 ng/mL) was present in 10.3% of men. Primary hyperparathyroidism was uncommon and present in only 21 men.

Baseline Characteristics by Quartiles of PTH

Table 1 shows baseline characteristics in the study population by quartiles of PTH. Elevated PTH was associated with age and with prevalent MI/stroke and many cardiovascular risk factors, including hypertension, renal dysfunction, hypertension, adiposity, AF, FEV1, C-reactive protein, and NT-proBNP. No association was seen with prevalent diabetes mellitus, blood glucose, or high-density lipoprotein cholesterol. Significant inverse associations were seen between PTH and 25OHD and blood calcium. These associations remained after adjustment for age. The age-adjusted correlations between PTH and biological risk markers are shown in Table 2.

| Table 1. Baseline Characteristics by Quartiles of Parathyroid Hormone (pg/mL) in 3728 Men Without HF |
|-----------------------------------|-------------------------------------------------|------------------|-------------------|
| Quartiles                          | 1 (<36.1)                                      | 2 (36.1–44.7)    | 3 (44.8–55.5)     | 4 (≥55.6)         |
| No. of men                         | n=932                                          | n=935            | n=928             | n=933             |
| Age, y                             | 67.9 (5.3)                                     | 68.2 (5.3)       | 68.7 (5.6)        | 69.7 (5.6)        | <0.0001 |
| % Smokers                          | 18.4                                           | 13.7             | 9.7               | 8.9               | <0.0001 |
| % Manual                           | 57.8                                           | 55.4             | 50.3              | 51.9              | 0.005   |
| % Inactive                         | 31.7                                           | 32.1             | 32.9              | 39.4              | 0.006   |
| % Heavy drinkers                   | 3.9                                            | 3.6              | 4.1               | 3.2               | 0.79    |
| % MI/stroke                        | 14.8                                           | 10.2             | 14.8              | 16.9              | 0.0003  |
| % Diabetes mellitus                | 13.6                                           | 12.9             | 10.7              | 13.4              | 0.21    |
| % Atrial fibrillation              | 1.3                                            | 2.7              | 3.7               | 5.6               | <0.0001 |
| % Renal dysfunction (eGFR <60 mL/min per 1.73 m²) | 13.1                                           | 11.5             | 14.6              | 21.5              | <0.0001 |
| % Use of antihypertensive          | 29.2                                           | 28.1.7           | 32.0              | 40.8              | <0.0001 |
| % Statins                          | 9.3                                            | 5.7              | 6.1               | 6.4               | 0.008   |
| % LVH                              | 8.6                                            | 5.8              | 7.7               | 8.7               | 0.07    |
| % Multivitamin supplement          | 33.2                                           | 31.0             | 28.2              | 24.7              | <0.0001 |
| BMI, kg/m²                         | 26.5 (3.6)                                     | 26.9 (3.6)       | 26.9 (3.5)        | 27.2 (3.8)        | 0.0006  |
| SBP, mm Hg                         | 145.9 (22.8)                                   | 148.3 (22.5)     | 149.8 (24.5)      | 153.1 (25.4)      | <0.0001 |
| Cholesterol, mmol/L                | 6.01 (1.09)                                    | 6.04 (1.05)      | 6.07 (1.06)       | 5.92 (1.08)       | 0.02    |
| HDL-C, mmol/L                      | 1.32 (0.34)                                    | 1.32 (0.33)      | 1.33 (0.34)       | 1.31 (0.35)       | 0.62    |
| Glucose, mmol/L*                   | 5.63 (5.22–6.16)                               | 5.63 (5.27–6.10) | 5.64 (5.25–6.07)  | 5.62 (5.26–6.09)  | 0.60    |
| Vitamin D*                         | 22 (16–28)                                     | 20 (14–26)       | 18 (13–24)        | 16 (11–23)        | <0.0001 |
| Phosphorus                         | 1.18 (0.15)                                    | 1.17 (0.15)      | 1.15 (0.16)       | 1.13 (0.16)       | <0.0001 |
| Calcium                            | 2.45 (0.09)                                    | 2.43 (0.09)      | 2.43 (0.09)       | 2.41 (0.10)       | <0.0001 |
| eGFR, mL/min per 1.73 m²           | 73.5 (13.7)                                    | 73.8 (11.9)      | 72.2 (11.4)       | 69.6 (13.3)       | <0.0001 |
| FEV1, L                            | 2.66 (0.64)                                    | 2.65 (0.65)      | 2.61 (0.65)       | 2.50 (0.67)       | <0.0001 |
| CRP, mg/L*                         | 1.44 (0.81–3.49)                               | 1.44 (0.74–3.27) | 1.54 (0.81–3.39)  | 1.72 (0.92–3.74)  | 0.04    |
| Heart rate, beats per min          | 65.3 (11.9)                                    | 65.5 (12.0)      | 64.9 (12.8)       | 66.6 (12.9)       | 0.03    |
| NT-proBNP, pg/mL*                  | 78 (40–155)                                    | 84 (43–170)      | 86 (45.5–185.5)   | 121.0 (59–291)    | <0.0001 |

Mean and SD unless specified. BMI indicates body mass index; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; FEV1, forced expiratory volume in 1 s; HDL-C, high-density lipoprotein cholesterol; LVH, left ventricular hypertrophy; MI, myocardial infarction; NT-proBNP, N-terminal probrain natriuretic peptide; and SBP, systolic blood pressure.

*Median and interquartile range.
distribution, and this pattern was seen in both men without MI/stroke and in men with MI/Stroke. The age-adjusted relative risk for the 4 quarters in all men was 1.00 (reference), 0.88 (0.61–1.25), 0.83 (0.58–1.19), and 1.72 (1.26–2.35) across increasing quarters. Adjustment for covariates did not alter the null finding in the middle 2 quarters. Because risk was only elevated in the top quarter, we presented the adjusted relative risk for the top quarter versus the rest of the cohort in Table 3. The increased risk associated with elevated PTH remained even after adjustment for age, smoking, physical activity, social class, alcohol intake, body mass index, high-density lipoprotein cholesterol, antihypertensive treatment, systolic blood pressure, eGFR, prevalent diabetes mellitus and stroke, heart rate, AF, LVH, C-reactive protein, and FEV1 (Table 3). Further adjustment for incident MI made little difference to the findings. Exclusion of men with chronic kidney disease strengthened the association. Adjustment for baseline NT-proBNP attenuated the relationship, but the increased risk remained significant (adjusted relative risk, 1.41; 1.08–1.83).

When examined separately in men with and without MI/stroke, the increased risk was seen in both men with and without MI after adjustment for variables in model 3. Exclusion of the small number of men with hyperparathyroidism made no difference to the findings. We investigated possible interactions with obesity. Elevated PTH was associated with increased risk in both obese (≥30 kg/m²) and nonobese men, although the association was stronger in obese men. The relative risk adjusted for factors in model 3 in Table 3 was 1.48 (1.12–1.97) and 2.76 (1.64–4.66) in nonobese and obese men, respectively. However, a test for interaction was not significant (P=0.14).

We also conducted a sensitivity analysis restricting incident cases to those with information on LVEF (n=142 cases). PTH showed positive associations of a similar strength to both HF with reduced EF (significantly) and HFpEF, although the association with HFpEF was not statistically significant possibly because of the small number of HFpEF cases (n=35). The adjusted hazards ratio for HF with reduced EF after adjusting for factors in model 3 (Table 3) was 1.92 (1.28–2.81), and the corresponding hazards ratio for HFpEF was 1.90 (0.95–3.81).

### 25OHD, Mineral Metabolism, and Incident HF

Table 4 shows the association between 25OHD, calcium, and phosphate with risk of HF. In contrast with the results for PTH, 25OHD, calcium, and phosphate showed no significant association with risk of HF (Table 4). We examined further
separately the risk of HF associated with those with severe 25OHD deficiency (<10 ng/mL). There was no increased risk even in this group of men (age-adjusted hazards ratio for <10 versus ≥10 ng/mL, 1.07; 0.67–1.71).

**Discussion**

In this study of older British men with no prevalent HF or primary hyperparathyroidism, elevated plasma PTH (>55.6 pg/mL) was associated with increased risk of HF, both in men with and without prevalent MI/stroke. No association was seen between 25OHD or mineral metabolism (calcium or phosphate) and risk of HF. Our finding on plasma PTH and HF confirms a previous report of an association between elevated PTH (>65 pg/mL), but not 25OHD with HF in older adults, and extends the findings to older adults with MI/stroke, which has not been previously assessed.

**PTH and Incident HF**

Few population studies have examined the relationship between PTH and HF. Two studies have shown elevated PTH to be associated with HF independent of known risk factors, including hypertension and renal dysfunction, whereas 1
study suggested the association to be present in obese subjects only.22 We have shown elevated PTH (>55.6 pg/mL) to be associated with increased HF risk in both men with and without established CVD (MI/stroke). Although the association appeared to be stronger in obese men, there was no evidence of an interaction. The increased risk associated with PTH and HF was not explained by traditional risk factors for HF, including AF and LVH, which has shown to be associated with PTH, an observation confirmed in the present study. We did not have information on AF during follow-up, and it is possible that a part of the association may have been mediated by the development of AF. Renal dysfunction is a common cause of secondary hyperparathyroidism. However, the association between PTH and HF was stronger in those with no evidence of chronic kidney disease in both men with and without MI/stroke.

PTH receptors are found in the myocardium, and the association between elevated PTH and HF particularly in the absence of chronic kidney disease could conceivably reflect PTH activity in the cardiac tissue. This suggestion would suggest a biological role for PTH in promoting symptoms of HF and consequently BNP expression, but this is speculative. PTH has been associated with NT-proBNP in this and other studies. The association between PTH and incident HF was partially attenuated by adjustment for baseline NT-proBNP, although there still remained a significant higher risk, which is consistent with findings from the Uppsala Study. NT-proBNP is secreted by cardiomyocytes in response to increased myocardial wall stress. The increase in NT-proBNP associated with PTH may reflect the effects of PTH on pathological LV remodeling and direct effects on cardiomyocytes resulting in higher LV wall stress and potential cardiac injury. In vitro studies have suggested a direct hypertrophic effect of PTH on cardiomyocytes. Alternatively, elevated PTH may be a consequence of ongoing subclinical myocardial stress and hence correlated with elevated natriuretic peptides. Our analysis, together with previous data, suggests that elevation of PTH before onset of HF is not attributable only to elevated natriuretic peptides.

Vitamin D and Incident HF
Vitamin D insufficiency was common in this population of older men. Over 85% of the men had 25OHD levels <30 ng/mL, levels deemed insufficient compared with 71% in the US...
Cardiovascular Health Study of older adults >65 years. These data are, therefore, broadly consistent, given differing study locations and known cross-laboratory differences in 25OHD assay calibration. Epidemiological evidence that vitamin D deficiency may be associated with HF has largely come from cross-sectional studies. Although some prospective studies have shown 25OHD deficiency to be associated with increased risk of HF, others have failed to find an association between vitamin D status and HF. In a US study of >40,000 adults (average age, 50 years), low 25OHD levels were associated with increased risk of HF events. In the Ludwigshafen Risk and Cardiovascular Health Study (aged 56–70 years) and the Third National Health and Nutrition Examination Survey (>35 years), 25OHD deficiency was associated with increased HF deaths. Importantly, neither of these 2 latter studies included nonfatal HF events and did not take incident MI into account. The differences in results could also be explained by the age differences between study populations; these earlier studies were generally conducted in younger people. In older adults, HFpEF is a common type of HF and is often not associated with MI. The Physicians’ Health Study (mean age, 58.6 years) and the European Prospective Investigation into Cancer and Nutrition-Potsdam study also showed no association between plasma vitamin D–binding protein or 25(OH)D3 with risk of HF. The finding that 25OHD deficiency is not associated with HF in older adults is consistent with the findings from several cross-sectional population studies that 25OHD is not associated with any biochemical conduction or echocardiographic outcomes.

Strengths and Limitations
Our study is not without some limitations. It was based on an older, predominantly white, male population of European extraction, so that the results cannot be generalized directly to women, younger populations, or other ethnic groups. The current findings are based on doctor-diagnosed HF; which is likely to underestimate the true incidence of HF in this study population. However, the determinants of HF in this study population (including obesity and NT-proBNP) generally accord with prior data and, therefore, suggest potential external validity for our findings. Adjustments were based on measurements at examination, and we had no information on incident AF. Information on echocardiogram measurements was not available in all men, and we were not able to differentiate systolic and diastolic HF for all men. However, a sensitivity analysis performed on the HF cases with information on EF suggested a similar association between PTH and both HF with reduced EF and HFpEF. Our biochemical assays were based on routine clinical assays and are, therefore, robust. However, our second-generation PTH assay may detect several PTH fragments including 1 to 84 PTH, 7 to 84 PTH, and N-PTH. The validity of the PTH levels reported in this study is supported by the fact that PTH levels were consistent with those reported in older populations and showed the expected patterns of association (eg, with calcium and vitamin D concentrations).

Conclusions
Elevated PTH, but not 25OHD or mineral metabolism, is associated with increased risk of HF in older men with and without established CVD, which was not explained by its association with known risk factors for HF. Further studies are now needed to elucidate the mechanisms underlying this association and, in particular, test for any evidence for a direct causal association (perhaps by harnessing the power of genetics) between PTH and HF.

Sources of Funding
The British Regional Heart Foundation (BHF) grant (RG/08/013/25942). Dr Welsh is supported by a BHF intermediate fellowship. Vitamin D and parathyroid hormone measurements and laboratory analyses were supported by Diabetes UK Project Grants.

Disclosures
None.

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**CLINICAL PERSPECTIVE**

Heart failure (HF) is a major epidemic and significant public health burden in our aging society. In recent years, much attention has turned to the role of mineral and bone metabolism in HF, specifically vitamin D deficiency and hyperparathyroidism, which is common in elderly population. Hyperparathyroidism and low vitamin D status have been implicated in the pathogenesis of HF. We examined the prospective associations between parathyroid hormone (PTH), circulating 25-hydroxyvitamin D, and markers of mineral metabolism and risk of incident heart failure (HF) in >3700 older men with and without established cardiovascular disease. Elevated PTH (>55.6 pg/mL; top quartile) was associated with significantly higher risk of incident HF after adjustment for lifestyle characteristics, diabetes mellitus, blood lipids, blood pressure, lung function, heart rate, renal dysfunction, atrial fibrillation, forced expiratory volume in 1 s, and C-reactive protein (hazards ratio, 1.66; 95% confidence interval, 1.30–2.13). The increased risk was seen in both men and without previous myocardial infarction or stroke (hazards ratio, 1.72; 95% confidence interval, 1.07–2.76; hazards ratio, 1.70; 95% confidence interval, 1.25–2.30, respectively). Elevated PTH was significantly associated with N-terminal probrain natriuretic peptide, a marker of left ventricular wall stress. By contrast, 25-hydroxyvitamin D and other markers of mineral metabolism, including serum calcium and phosphate, showed no significant association with HF after adjustment for HF for age. Elevated PTH is associated with increased risk of HF in both older men with and without myocardial infarction/stroke. Further studies are now needed to elucidate the mechanisms underlying this association and to evaluate whether PTH-modifying therapies may reduce risk of developing heart failure.
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Circ Heart Fail. 2014;7:732-739; originally published online August 7, 2014;
doi: 10.1161/CIRCHEARTFAILURE.114.001272
Circulation: Heart Failure is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 1941-3289. Online ISSN: 1941-3297

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